Chronic myeloid leukemia stem cells.

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Public Summary:

Scientific Abstract:
Although rare, chronic myeloid leukemia (CML) represents an important paradigm for understanding the molecular events leading to malignant transformation of primitive hematopoietic progenitors. CML was the first cancer to be associated with a defined genetic abnormality, BCR-ABL, that is necessary and sufficient for initiating chronic phase disease as well as the first cancer to be treated with molecular targeted therapy. Malignant progenitors or leukemia stem cells (LSCs) evolve as a result of both epigenetic and genetic events that alter hematopoietic progenitor differentiation, proliferation, survival, and self-renewal. LSCs are rare and divide less frequently, and thus, represent a reservoir for relapse and resistance to a molecularly targeted single agent. On subverting developmental processes normally responsible for maintaining robust life-long hematopoiesis, the LSCs are able to evade the majority of current cancer treatments that target rapidly dividing cells. Enthusiasm for the enormous success of tyrosine kinase inhibitors at controlling the chronic phase disease is tempered somewhat by the persistence of the LSC pool in the majority of the patients. Combined therapies targeting aberrant properties of LSC may obviate therapeutic resistance and relapse in advanced phase and therapeutically recalcitrant CML.

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